

The Structural Biology Community in South Africa and it's links to the ESRF

Prof Wolf-Dieter Schubert

University of Pretoria

Department of Biochemistry, Genetics and Microbiology



Trevor Sewell



Jeremy Woodward



Ed Sturrock



Kelly Chibale



Erick Strauss



Albie van Dijk



Wolf-Dieter Schubert



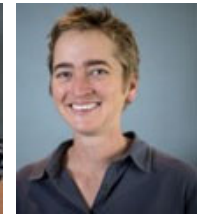
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UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA



Paul Abidemo Kappo



Lynn Morris



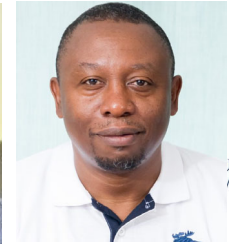
Penny Moore



Thandeka Moyo



Yasien Sayed



Ikechukwu Achilonu



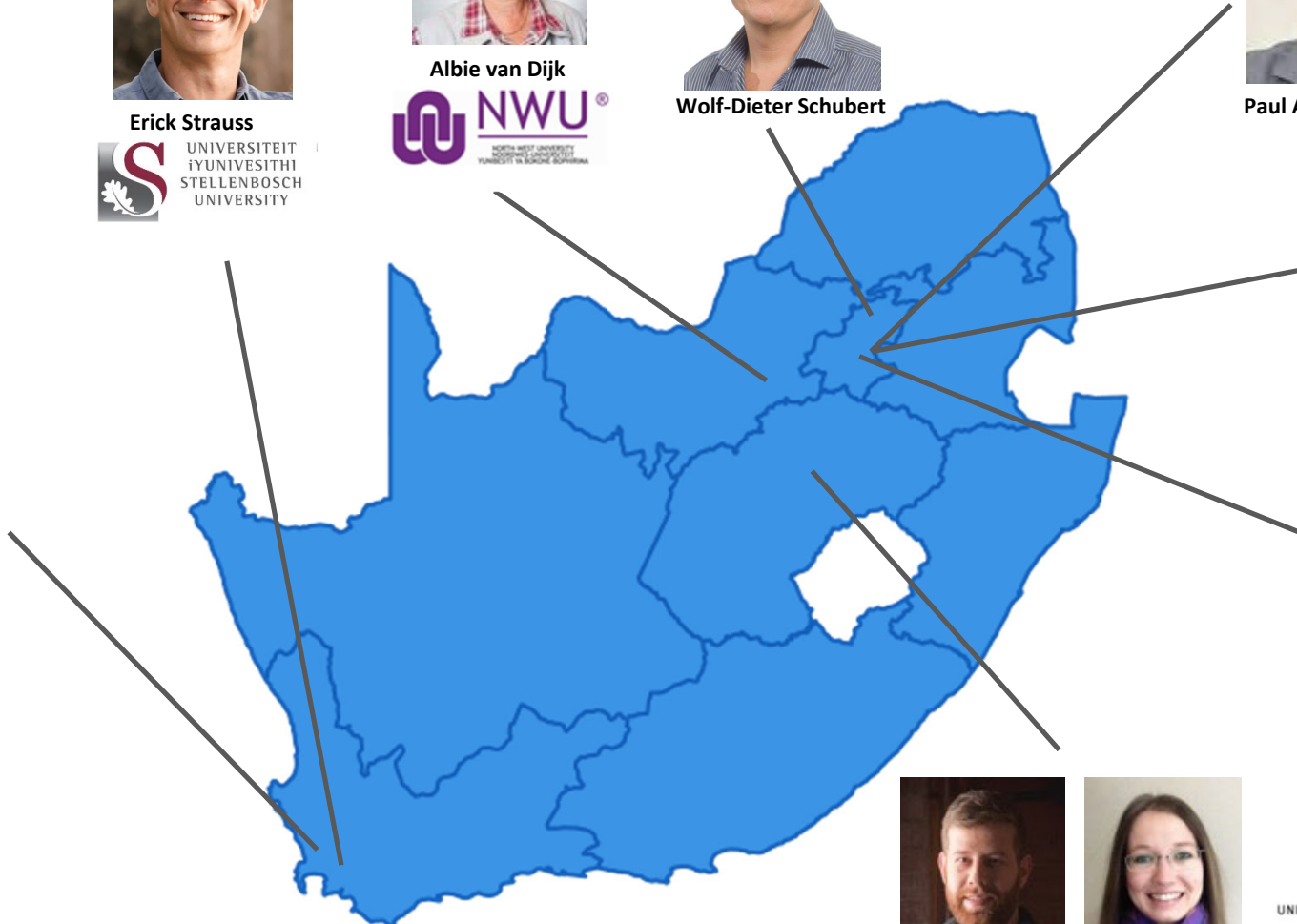
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WITWATERSRAND
JOHANNESBURG

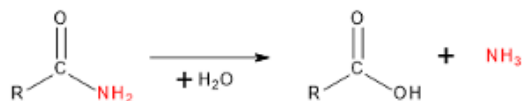


Dirk Opperman



Carmien Tolmie





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Trevor Sewell



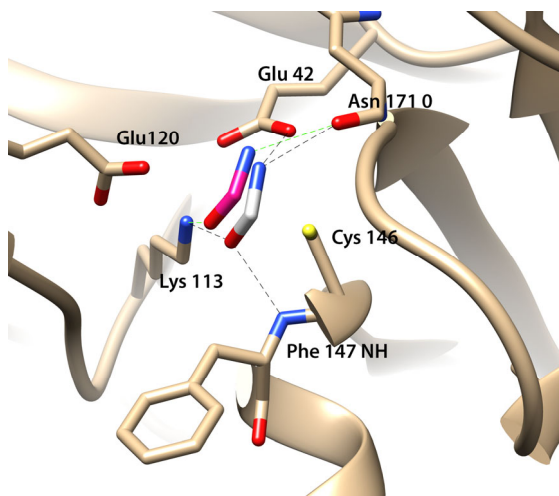
Stanley
Makumire



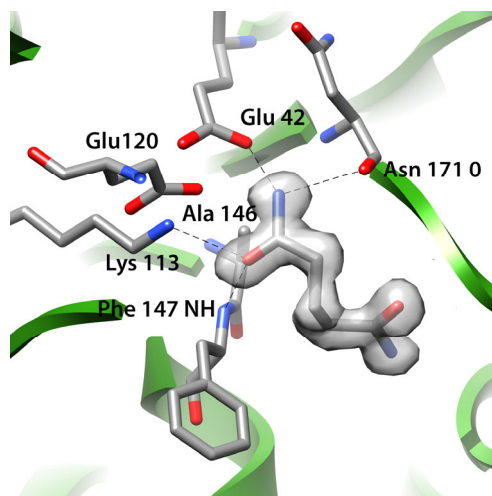
Philip Venter

Substrate position and hydrolysis in the amidases

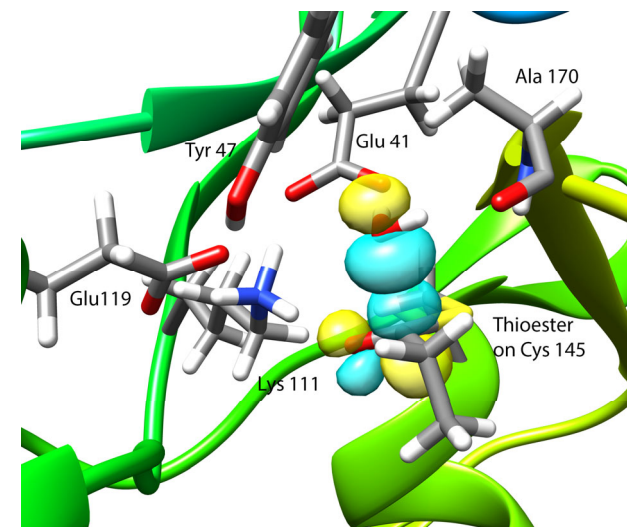
Many issues bedevil an understanding of the amidase mechanism especially the locations of the substrate and the catalytic cysteine



Docking of 14 amides predicts the substrate amide hydrogen bonding in both WT and C146A variants. The involvement of the backbone carbonyl of Asn 171 was unknown.



Crystal structure of glutaramide in the C146A amidase variant verifies the prediction. This location leads to the formation of a thioester Intermediate.



Quantum mechanical calculations show orbital overlap with a water positioned by the carboxyl of the active site glutamate and the same backbone carbonyl leading to hydrolysis and product formation.



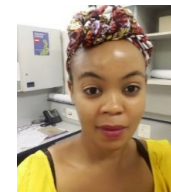
Kelly Chibale



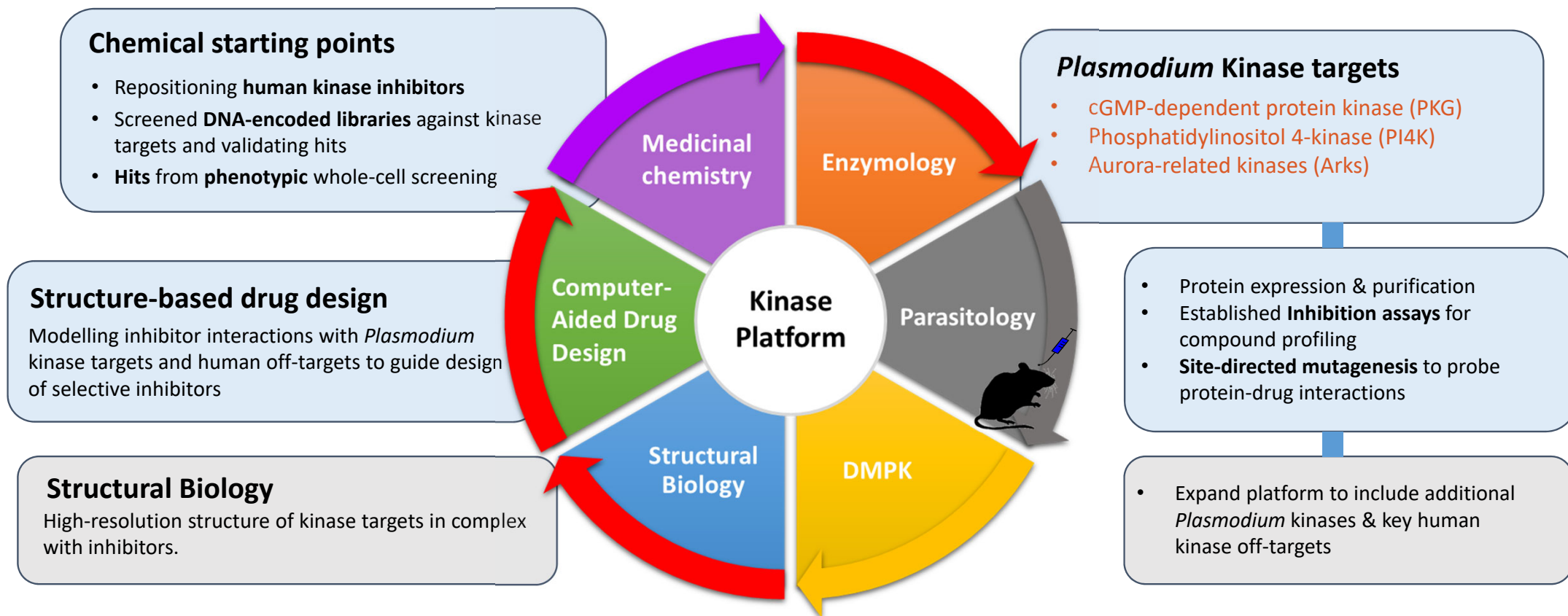
Lauren Arendse



Andani Mulelo



Establishing a *Plasmodium* kinase platform for target-based malaria drug discovery

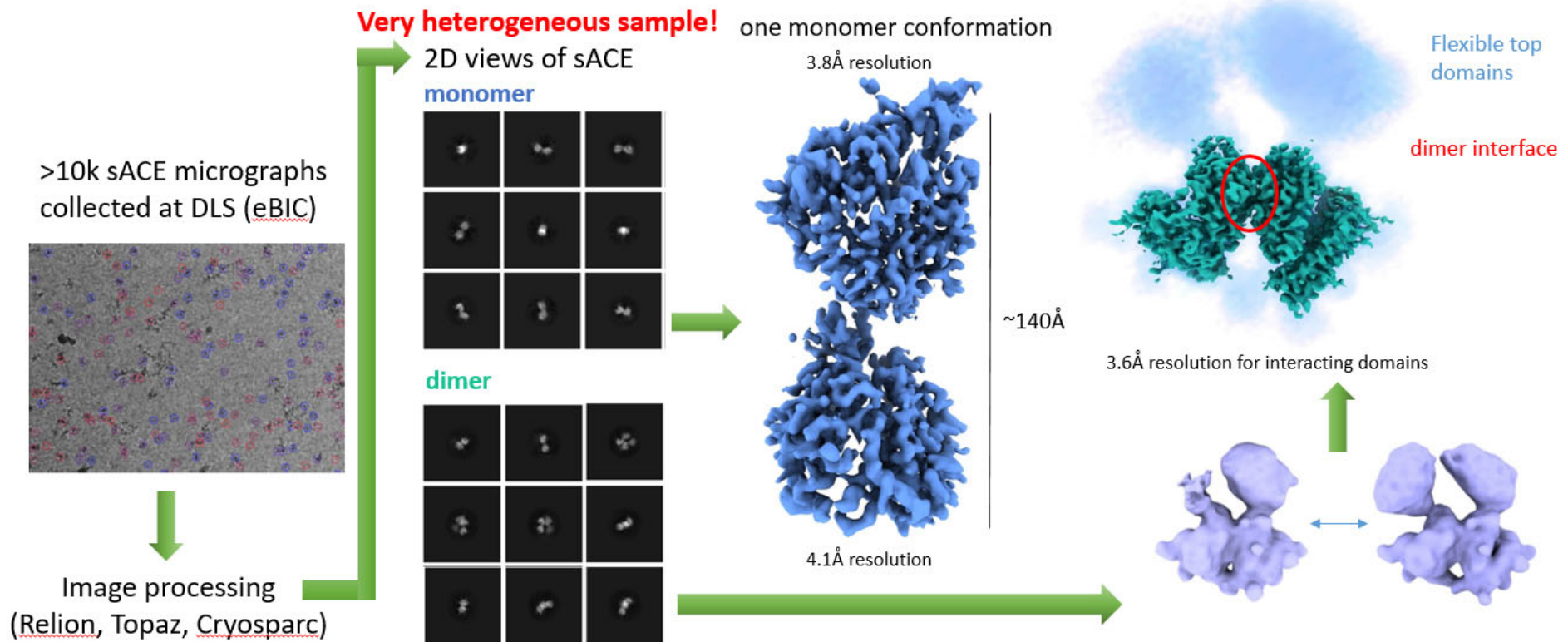




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Angiotensin-converting enzyme





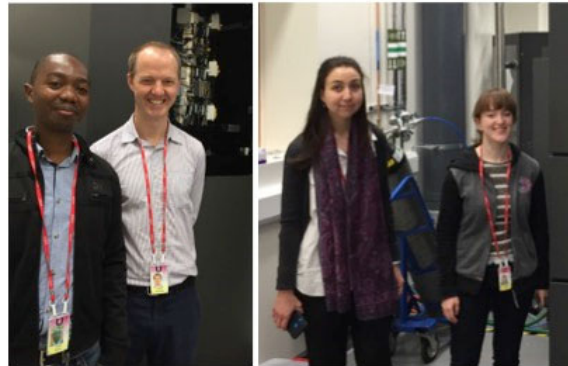
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Developing Expertise in single particle electron microscopy of Biological Macromolecules.



Jeremy Woodward

Jeremy Woodward



World's first published **nitrilase structure**

First published **close-to-atomic resolution cryo-EM structure** in Africa



Erick Strauss



Anton Hamann

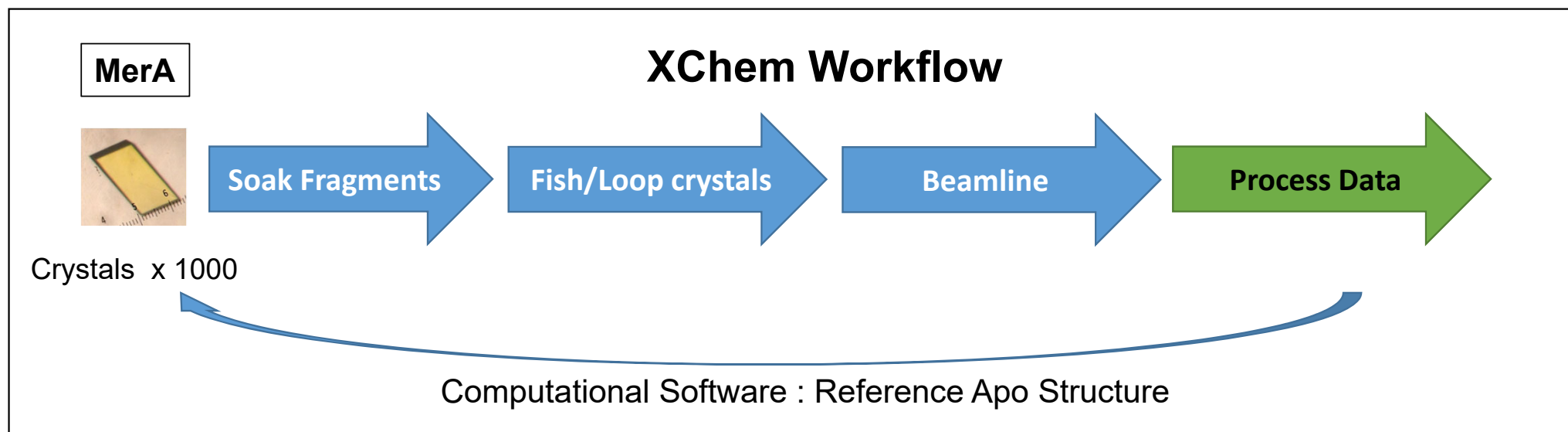


Blake Balcomb

Targeting Pantothenate and Coenzyme A Biosynthesis

- XChem (X-ray structure-accelerated, synthesis-aligned fragment-based MedChem)

Frank von Delft (SGC-Oxford, Diamond Light Source U.K.)



OPEN Biochemical and structural
insights into the cytochrome P450
reductase from *Candida tropicalis*

Ana C. Ebrecht^{1,2}, Naadia van der Bergh^{1,2}, Susan T. L. Harrison^{2,3}, Martha S. Smit^{1,2},
B. Trevor Sewell^{1*} & Diederik J. Opperman^{1,2*}



Dirk Opperman



Carmien Tolmie

Cytochrome P450 monooxygenases

- CYPs are heme-thiolate enzymes that catalyse a range of reactions
- Focus on CYPs that perform regioselective hydroxylations of fatty acids and alkanes
→ aim is to gain insight into how the **active site determines the regioselectivity**



Rodolpho
Do Aido-
Machado



Tiyani (T)



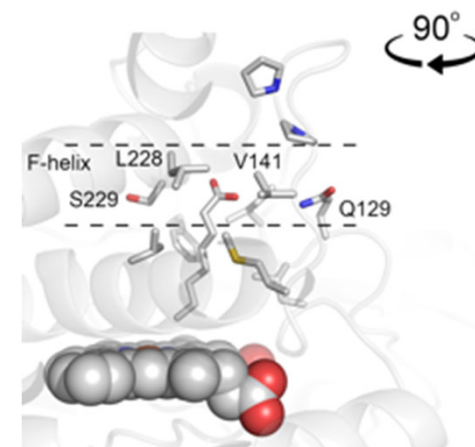
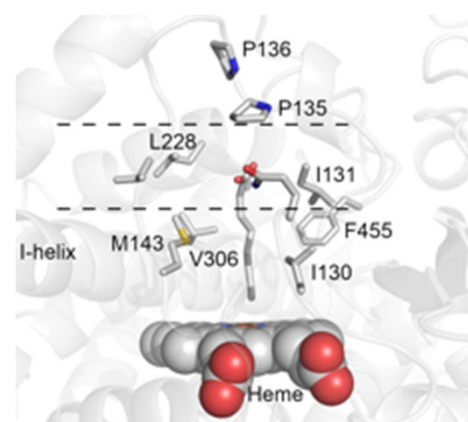
Cheri
Jacobs



Jasmin
Aschenbrenner



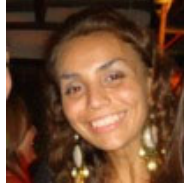
Ana Ebrecht



Non-structural protein 4 (NS4) from African horse sickness virus



Albie van Dijk



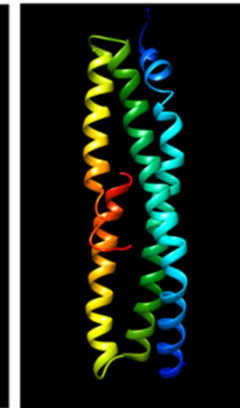
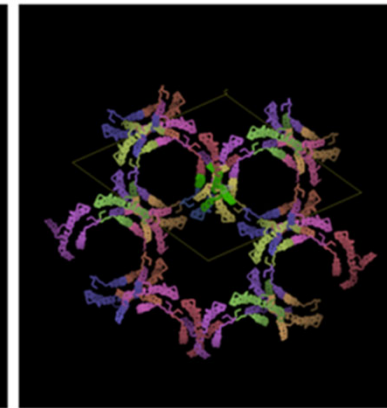
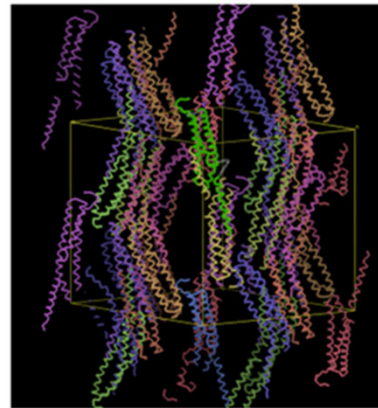
Ana Ebrecht



- NS4 is a key virulence factor → target for a vaccine development
- Function of NS4 in AHSV unclear
- Understanding the protein structure **can shed light on the molecular virulence mechanism and host-virus interaction**

Data collection statistics

Unit cell parameters (a b c, α β γ)	101.084 101.084 113.872 90 90 120
Space group	P6 ₃ 22 or P6 ₁ 22
Resolution range (Å)	∞ – 3.36 (3.40 – 3.36)
Completeness (%)	99.8 (100.0)
< I/ σ >	18.93 (1.37)
R-merge	0.1021 (0.9470)
CC _{1/2}	0.93(0.35)



- Data collected for a truncated version of the protein
- Coiled-coil structure
- Analysis of the structure to predict interaction with DNA and other proteins



Lynn Morris



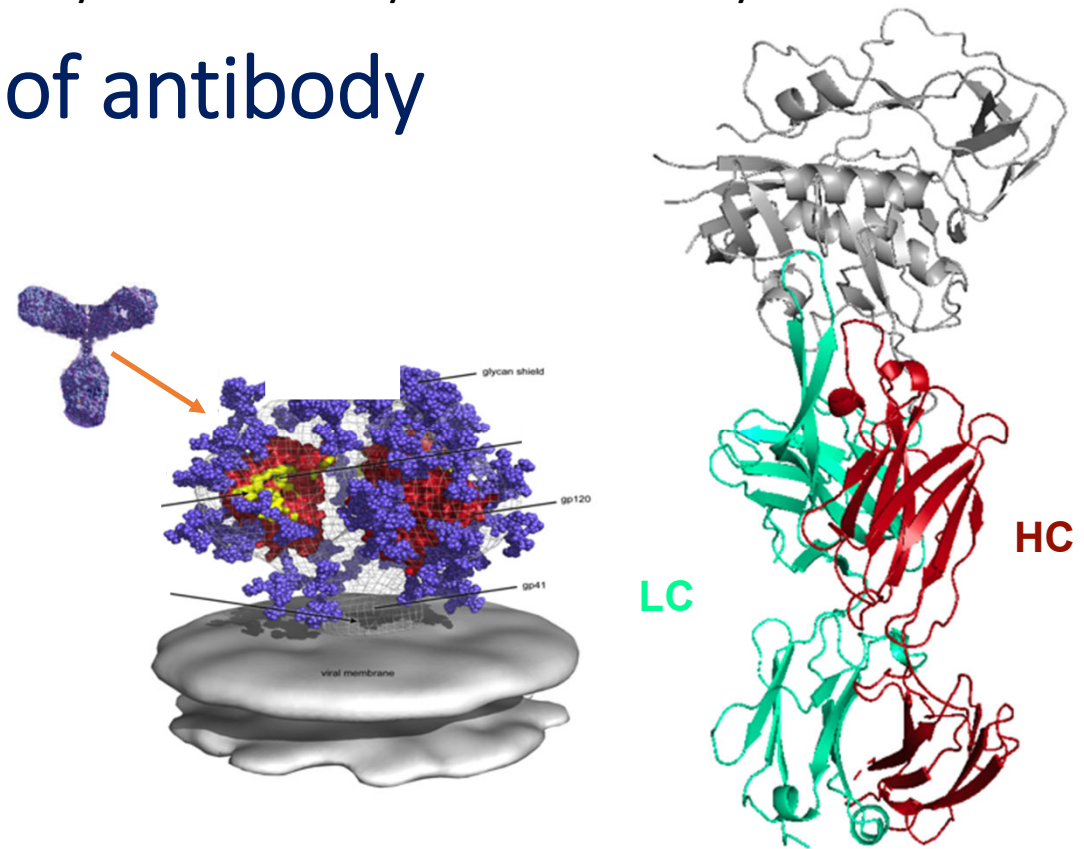
Penny Moore



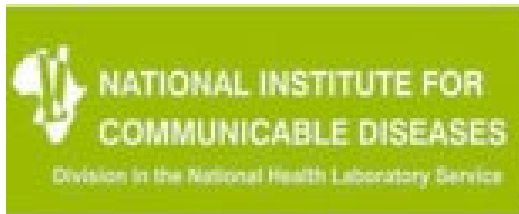
Thandeka Moyo

Structural characterization of antibody lineages from single donor

- CAP314 – HIV-infected donor who developed bNAbs within 2 years post-infection
- Isolated and characterized three antibody lineages
- Crystallized the antibody in complex with a gp120 envelope protein (3.3 Å structure)










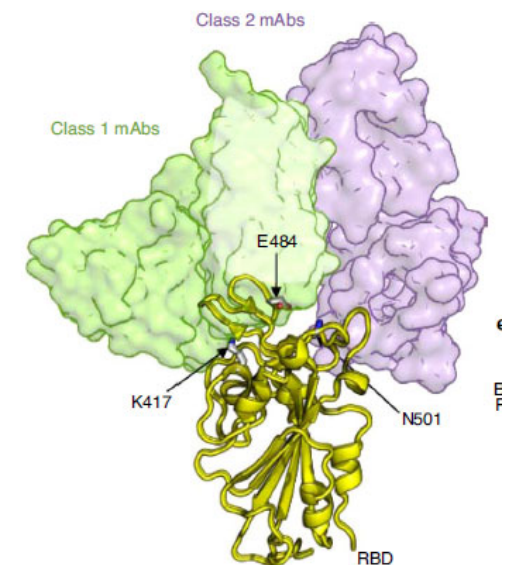
Adapted from Burton et al., 2012



Constantinos Kurt Wibmer

SARS-CoV-2 501Y.V2 escapes neutralization by South African COVID-19 donor plasma

Constantinos Kurt Wibmer¹, Frances Ayres¹, Tandile Hermanus¹, Mashudu Madzivhandila¹, Prudence Kgagudi¹, Brent Oosthuysen¹, Bronwen E. Lambson^{1,2}, Tulio de Oliveira³, Marion Vermeulen⁴, Karin van der Berg ^{4,5}, Theresa Rossouw⁶, Michael Boswell ⁷, Veronica Ueckermann⁷, Susan Meiring ¹, Anne von Gottberg^{1,8}, Cheryl Cohen^{1,9}, Lynn Morris ^{1,2}, Jinal N. Bhiman ^{1,10,11} and Penny L. Moore ^{1,2,11} 



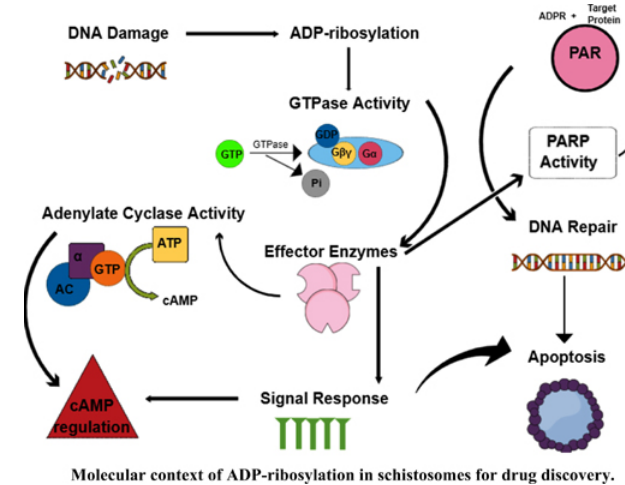
NATURE MEDICINE | VOL 27 | APRIL 2021 | 622–625



Paul Abidemo Kappo



Dr Priscilla Masamba



Previously: University of Zululand

President: South African Society of Biochemistry and Molecular Biology (SASBMB)

Schistosomiasis

- caused by parasitic worms (schistosomes) endemic in more than 78 countries.
- ~4 million people are infected in South Africa alone.
- The disease involves the freshwater snail *Bulinus africanus* as an intermediate host.
- Mostly occurs in rural areas where people are infected by exposure to infested water.

Partial structure of the Schistosomiasis (Bilharzia) G4LZI3 universal stress protein



Yasien Sayed



Ikechukwu Achilonu



Ramesh Pandian



Heini Dirr

Molecular & Biochemical Parasitology 240 (2020) 111319



Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Molecular & Biochemical Parasitology

journal homepage: www.elsevier.com/locate/molbiopara



Molecular basis of inhibition of *Schistosoma japonicum* glutathione transferase by ellagic acid: Insights into biophysical and structural studies

Blessing O. Akumadu, Ramesh Pandian, Jessica Olfson, Roland Worth, Monare Thulo, Tshireletso Mentor, Sylvia Fanucchi, Yasien Sayed, Heini W. Dirr, Ikechukwu Achilonu *

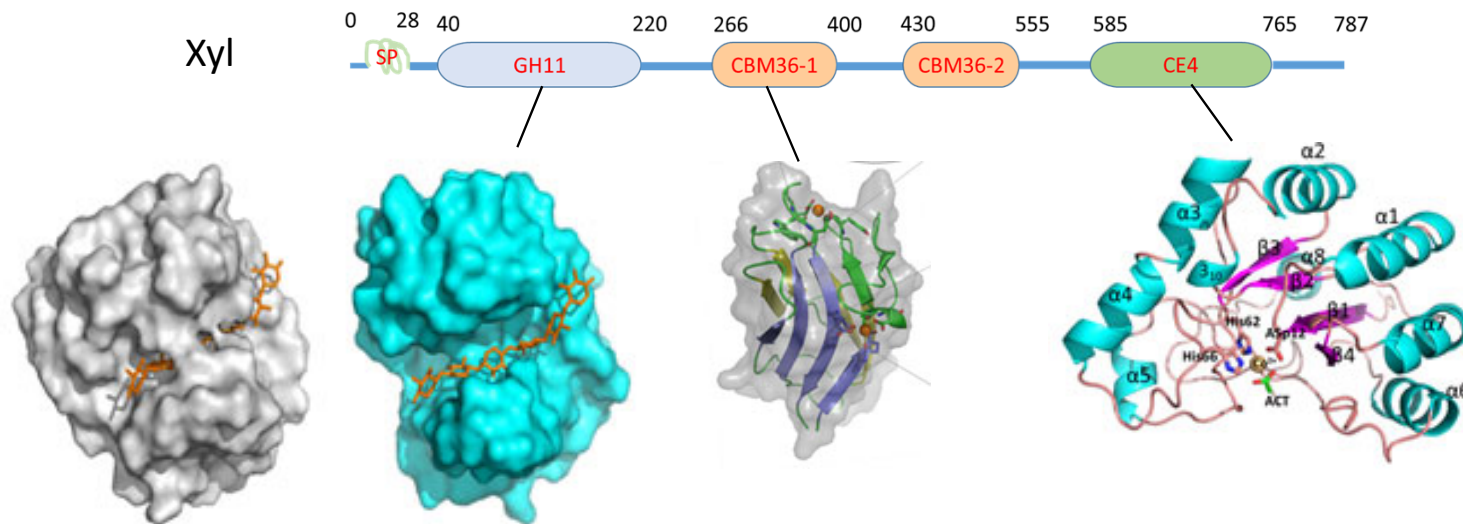
Protein Structure-Function Research Unit, School of Molecular and Cell Biology, Faculty of Science, University of the Witwatersrand, Johannesburg 2050, South Africa



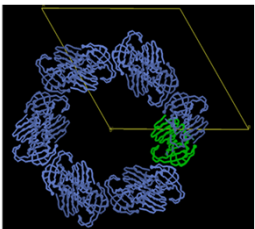
Structural characterization of a multidomain xylanase from a termite metagenome



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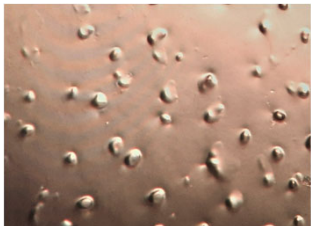
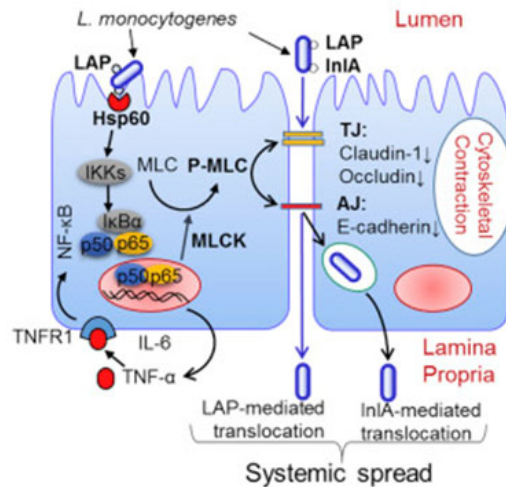


Valentine Anye

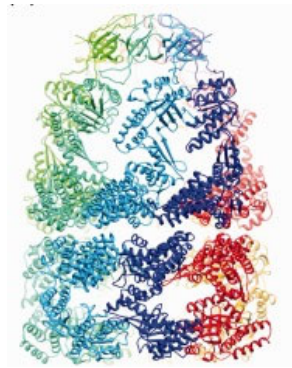


- Individual domains have been analysed structurally and kinetically.
- pH and temperature optima of the two catalytic domains indicate Xyl to be a mesophilic enzyme working at neutral pH.
- Despite initial indication of interdependence of domains, data indicate distinct domains connected by flexible linkers.

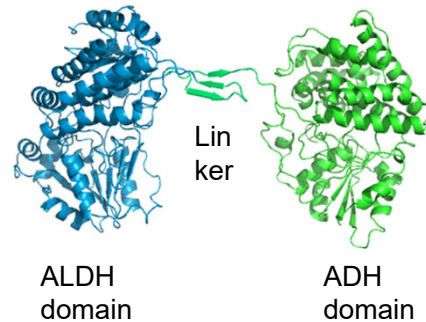
Characterizing the interaction of HSP60 with listerial adhesion protein (LAP)



LAP Microcrystals



Mitochondrial HSP60 (GroEL)



Bifunctional alcohol and aldehyde dehydrogenase (AdhE)



Vukosi Munyai



Clare Boswell

- Both HSP60 and LAP (AdhE) are normally located far away from the cell surface.
- Both proteins have **moonlighting functions in listerial infection.**
- Proposed to form a complex on the surface of epithelial cells.



Synchrotron Techniques for African Research and Technology 2018 – 2021

- Collaboration of 25 African and British research groups using synchrotron techniques.
- Material Science and Structural Biology
- Support for Postdoctoral Fellows, laboratory funding, travel.
- Remote access for data collection and centralised sample transport .
- Major impact on Structural Biology in South Africa

Links to ESRF



Joint German, Russian, South African BAG.

- Members: Trevor Sewell and Wolf-Dieter Schubert (open to others)
- ESRF covers costs of two to three travelling scientists
- Used synchrotron 2010 to 2017
- Various papers published and structures deposited in Protein Data Bank

Recent improvements:

- ESRF covers costs for sample shipment
- Remote data collection now possible

